AUSTRALIA

Patents Act 1990

IN THE MATTER OF
US Patent Application No.
09/446,109 by The
University of Queensland

STATUTORY DECLARATION UNDER RULE 132

I, Vivien Bedford Santer of 21 High Road, Camberwell, in the State of Victoria 3124, Commonwealth of Australia, do solemnly and sincerely declare as follows:

1. I am a registered patent attorney and a member of the firm of Griffith Hack of 509 St Kilda Road, Melbourne, in the State of Victoria 3004, Commonwealth of Australia (hereinafter referred to as my firm), which is acting on behalf of the assignee of the present application, and I am the patent attorney primarily responsible for prosecution of this application in Australia and in other countries. I am responsible for instructing the applicant's United States attorneys, Messrs. Oblon Spivak McClelland Maier & Neustadt PC.

2. I have also worked in the field of medical research for many years, including several years of research in the field of connective tissue and arthritis research. A copy of my *curriculum vitae* is now shown to me, and is annexed hereto as Exhibit VBS-1.

3. I have read and understood the Office Action dated 18 December 2003 issued in respect of this application.

4. In this Office Action, the Examiner has raised an objection under Section 112 first paragraph that the specification does not provide an enabling disclosure in respect of a method of treating an inflammatory condition, an arthritic condition, or an inflammatory arthritis, comprising the step of administering an effective amount of a compound of the invention to a mammal in need thereof.

5. From January 1974 to November 1976 I was a Senior Tutor in the Department of Biochemistry at Monash University in Melbourne, Australia and worked in the Connective Tissue Group of the Department. This group had for a number of years used carrageenin-induced arthritis in rabbits as a model system for rheumatoid arthritis. Members of this research group were investigating various aspects of pathological changes in cartilage morphology and metabolism, and the group had published many papers on results obtained using this model.

6. From 1980 to 1981 I was a post-doctoral fellow in the Joint Diseases Laboratory at the Shrine's Hospital for Crippled Children in Montreal, Canada, *inter alia* carrying out studies on protoglycans in human articular cartilage.

7. During these two periods I was familiar with the scientific literature in the field, and maintained an awareness of new developments. In particular, I was aware of the animal model systems which were being used in the study of rheumatoid arthritis and other inflammatory arthritides. For example, I was aware of the use of the seaweed polysaccharide carrageenin to induce a variety of inflammatory responses. These included granulomas induced by subcutaneous injection of carrageenin; footpad oedema induced by sub-plantar injection of carrageenin into the footpad of rats; and adjuvant-induced arthritis in rats or mice. All of these models used small rodents, and consequently the types of study which could be carried out were limited by the size of the joint.

8. For this reason, the laboratory at Monash University had adopted a model of arthritis induced by intra-articular injection of carrageenin into rabbits. This model had already been used at Monash University for some years before I joined the laboratory, and I myself used this model. I was co-author on two publications in which this model

was used, and copies of abstracts of these publications are annexed hereto as Exhibit VBS-2.

9. This model has only partially been superceded by antigen-induced arthritis, which was initially described in 1962. I was involved in introducing this model to the laboratory at Monash University in about 1975-1976, and I was a co-author of a publication reporting studies using the antigen-induced arthritis model in rabbits. A copy of the abstract of this publication is annexed hereto as Exhibit VBS-3.

10. Through my reading of the scientific literature and through my subsequent work as a patent attorney in respect of patent applications relating to methods and therapeutic agents for the treatment of rheumatoid arthritis and other inflammatory arthritides, I was aware well before the priority date of the present application that collagen-induced arthritis is regarded as the most closely related form of antigen-induced arthritis to rheumatoid arthritis. However, I was aware both from the literature and from the work of my colleagues at Monash University that collagen is a protein which is very difficult to prepare in highly-purified form. Consequently I was aware that other antigens, such as ovalbumin or albumin are much cheaper and easier to obtain, and that such antigens are more commonly used in the art, at least in preliminary studies.

11. I was also aware that carrageenin-induced footpad oedema is a widely used standard assay for assessing the anti-inflammatory activity of candidate drugs for this indication, and that adjuvant-induced arthritis is also widely used for this purpose. I was aware that these assays are widely regarded in the art as being predictive of efficacy in the treatment of inflammatory conditions, including inflammatory arthritides.

12. For example, the rat footpad model was used for the initial demonstration of the anti-inflammatory activity of indomethacin and piroxicam, two well-known non-steroidal anti-inflammatory drugs (NSAIDs) which are very commonly used in the treatment of rheumatoid arthritis and other inflammatory arthritides, such as psoriatic arthritis and ankylosing spondylitis. Proprietary information sheets referring to this which were found on the World Wide Web are annexed hereto as Exhibit VBS-4.

13. I therefore consider that long before the priority date the experimental models described in the specification in respect of the present application were widely known in the art, and regarded as reasonably predictive of results in humans.

And I make this solemn Declaration by virtue of the Statutory Declarations Act 1959, and subject to the penalties provided by the Act for the making of false statements in Statutory Declarations, conscientiously believing the statements contained in this Declaration to be true in every particular.

DECLARED at Melbourne this 13th day of May 2004

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Vivien Bedford Santer

Before me: .....

SALLY ANN SHRIMPTON
3rd Floor, 509 St. Kilda Rd, Melbourne 3004
A current practitioner within the meaning
of the Legal Practice Act 1996.

A person empowered to witness
Statutory Declarations under the
laws of the State of Victoria,
Commonwealth of Australia